REMARKS

Rejections - 35 USC § 103

Claims 1-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Barnes (U.S. Patent No. 4,721,723) in view of Saches (U.S. Patent No. 6,068,856) and Karehill (U.S. Patent No. 6,605,303).

According to the Office Action, Sachs and Karehill disclose formulations whose active ingredient is acid labile drugs such as pantoprazole and omeprazole, and Applicant's claimed invention could be easily made from the combination of the cited art, because the paroxetine hydrocholoride hemihydrate, the active ingredient of Applicant's claimed invention, is also an acid labile drug and the formulation of Applicant's claimed invention and those of Saches and Karehill. Therefore, the Office Action concludes that those skilled in the art would be motivated to formulate paroxetine hydrochloride hemihydrate as an acid labile drug using the formulations of Sachs and Karehill. Further, the Office Action contended that those skilled in the art would have had a reasonable expectation of success in producing Applicant's claimed invention from the teachings of Sachs and Karehill. Applicant respectfully disagrees.

1. Paroxetine is not an acid-labile drug

The Office Action's ground for the obviousness rejection is that the active ingredient of Applicant's claimed invention, paroxetine hydrochloride hemihydrate, is an 'acid labile drug' like as pantoprazole or omeprazole and thus a person in the field would have applied the formulation technique of Sachs and Karehill to paroxetine hydrochloride hemihydrate, and would have have a reasonable expectation of success. However, contrary to the Office Action's conclusion, paraxetine is not an acid labile drug like as pantoprzole and omeprazole.

At column 1, lines 30-33, Barnes states that it is preferred that paroxetine is used as a therapeutic agent in the form of an acid addition salt due to its basicity. However, in view of the fact that Sachs uses omeprazole as a Mg salt and Karehill uses pantoprazole as a Na salt, it is clear that paroxetine is not an acid labile drug like pantoprazole and omeprazole. Also, the fact that paroxetine is not an acid labile drug will be very clear from Attachment 1. At line 4 from the bottom of page 1395, Attachment 1 states that paroxetine was relatively stable under acid, base,

and heat. Also, it states that "paroxetine was found to be stable in all pH buffer solutions for 30 d" and "[p]hotolysis of paroxetine was accelerated by increasing pH" (see line 11 from the bottom of right column on page 1395). Further, it concludes that paroxetine was shown to be stable under dark conditions in solutions for at least 30 d, yet was found to be degraded rapidly by simulated sunlight. Accordingly, Sachs and Karehill are not applicable to paraxetine hydrochloride hemehydrates since paroxetine hydrochloride hemihydrate is not an acid labile drugs. Therefore, it cannot be concluded that those skilled in the art would be motivated to formulate paraxetine hydrochloride hemehydrates using technique disclosed by Sachs and Karehill.

2. The object of the introduction of the enteric coating layer is different

Further, Applicant's claimed invention and Sachs and Karehill have different purposes for introducing enteric coating layers. Therefore, the effect of Applicant's claimed invention can be achieved by Sachs and Karehill with a reasonable expectation of success. In Applicant's claimed invention, the purpose for the introduction of enteric coating layer is not because paroxetine is a type of acid labile drugs, but is to reduce side effects and increase tolerability (see Attachment 2). In other words, because the adverse effect of the paroxetine IR tablet occurs frequently, the enteric coating layer was introduced to delay the release in order to avoid such adverse effect. However, the purpose of the enteric coating layer in Sachs and Karehill was to securely deliver the acid labile drug to the intestine through the acidic atmosphere. Therefore, because the purposes for the enteric coating layer are different, the effect of Applicant's claimed invention can be achieved by Sachs and Karehill with a reasonable expectation of success.

3. The object of the introduction of the separation layer is different

Sachs and Karehill also have a separation layer. But their purpose of introducing the layer is different from Applicant's claimed invention. Especially, Applicant had found that when an enteric coating layer is directly introduced on a sustained release tablet core containing paroxetine, the release behavior of the tablet significantly changes. Especially Applicant found that such release behavior of the tablet is largely subject to GET. That is, drug release behavior

of such tablet is not regulated as originally designed after the tablet is transferred into the intestines, with regard to the residence time of the tablet in the stomach.

This is fully stated in Applicant's specification and can be seen from the examples of Table 2. According to Table 2, the drug release rate significantly decreased because of significant changes in the originally designed drug release behavior when a sustained release tablet core comprising paroxetine was directly introduced with an enteric coating layer when tested for 2 hours in an acidic environment (of the stomach) and then transferred to a neutral condition (of intestines)].

Applicant closely examined a way to regulate such change in the drug release and reached a conclusion that this problem could be prevented if a special separation layer is introduced between a tablet core comprising paroxetine and an enteric coating layer in a way that the core is completely enclosed. This is an important feature of the claimed invention.

Sachs and Karehill, on the other hand, do not recognize these problems. For example, according to Karehill, between the core material and the outer enteric coating layer, a separating layer can be added for the purpose of using a separation layer to improve the active chemical ingredient's stability and/or enhance the formulation properties (column 10, line 5-9). Therefore, Sachs and Karehill do not teach using a separation layer to solve the unique problem in paroxetine's enteric coating.

4. The rejection is improper

The Office Action's conclusion that the claimed invention can be easily made by a person of ordinary skill in the art by using the formulations disclosed in Barnes in view of Saches and Karehill is based on the premise that paroxetine is an acid labile drug. However, as stated above, paroxetine is not an acid labile drug. Therefore, the Office Action's conclusion is incorrect. Further, the formulation of Saches and Karehill, especially regarding the separation layer's purpose, is different from the claimed invention. Hence, a person skilled in the art cannot easily arrive at the separation layer of the claimed invention from Saches and Karehill.

In light of the foregoing remarks, this application is considered to be in condition for allowance, and early passage of this case to issue is respectfully requested. If necessary to effect

a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 07-1850.

Respectfully submitted,

Date: March 12, 2010

/Song Zhu, Reg. No. 44,420/

Squire, Sanders & Dempsey L.L.P.
One Maritime Plaza
Suite 300
San Francisco, CA 94111
Facsimile (415) 393-9887
Telephone (415) 954-0241
szhu@ssd.com

Song Zhu, Ph.D.
Attorney for Applicant
Reg. No. 44,420